From rigid to flexible: graphene-based extracellular sensors

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Abstract

Having a chip with a large array of sensitive, fast and linearly responsive, and stable recording sites is a holy grail of biological sensors for the recording of extracellular potentials from electrogenic cells, especially neurons. Such kinds of chips have been and still being fabricated and used. But these chips are mostly based on silicon and silicon technology. The main drawback of these devices is their inflexibility and high Young's modulus. Therefore, such devices are unusable if one wants to go into flexible *in-vivo* sensors.

Graphene, considering its overall properties [1], seems to be the cornerstone for bringing high tech of microelectronics into flexible shell and into biology. The graphene field effect transistors (GFETs) show great performance in terms of response time (<µs) and linearity (ΔV_{GS} into ΔI_{DS}). At the same time, the devices show comprehensively high sensitivity (transconductance over 11 mS/V) and overall stability.

In this work we generally compare GFETs fabricated on rigid (silicon and sapphire) and flexible (polyimide) substrates. The devices show truly different performance: silicon shows the worst sensitivity, while sapphire and polyimide have comparably similar great performance, although polyimide is a flexible substrate.

We can record extracellular signals with the rigid substrate graphene FETs (Fig. 1) and even calculate their propagation through the chip (Fig. 2). We can even record the "reaction" of the cellular layer on special drugs and chemicals: addition of 20 µL of NorA into the cell culture medium doubles their beating frequency, while addition of a surfactant (SDS) results in a slow dissolving of the cellular layer and therefore disappearance of the beating (Fig. 2c). But is this a huge step forward? This had been done years ago with silicon FETs [2] and multi electrode arrays (MEAs) [3].

In order to go further we have fabricated similar GFETs on flexible polyimide (PI) substrate (Fig. 3a). These devices, while difficult to perform the usual *in-vitro* tests, due to bonding problems, are easily implemented for *in-vivo* measurements. As an intermediate stage we performed the recording of the actual heart tissue slice with such chip (Fig.3b) and got very large signal-to-noise (SNR) recorded action potentials (Fig. 3c).

References

[1] A.C. Ferrari et al., Nanoscale, **11** (2015), 4598-4810
[2] J.F. Eschermann, R. Stockmann, M. Hueske, X. T. Vu, S. Ingebrandt and A. Offenhäusser, Applied Physics Letters, 95 (2009), 083703
[3] J. Hescheler, M. Halbach, et al., Journal of Electrocardiology, **37** (2004), 110-116.

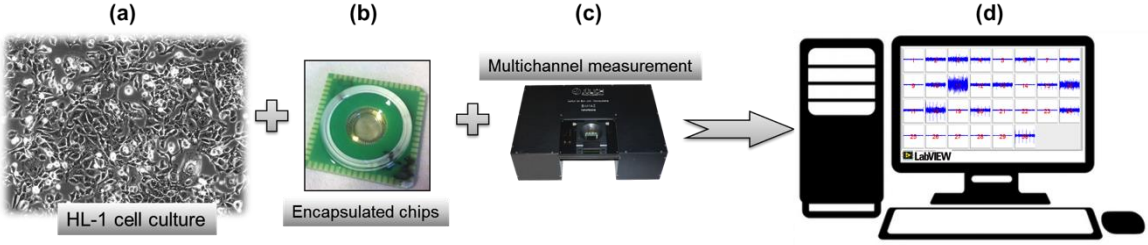

Figure 1 The cell culture (a) on a chip (b) is recorded via the multichannel measurement set-up (c), manipulated via PC with Lab-View based software (d)

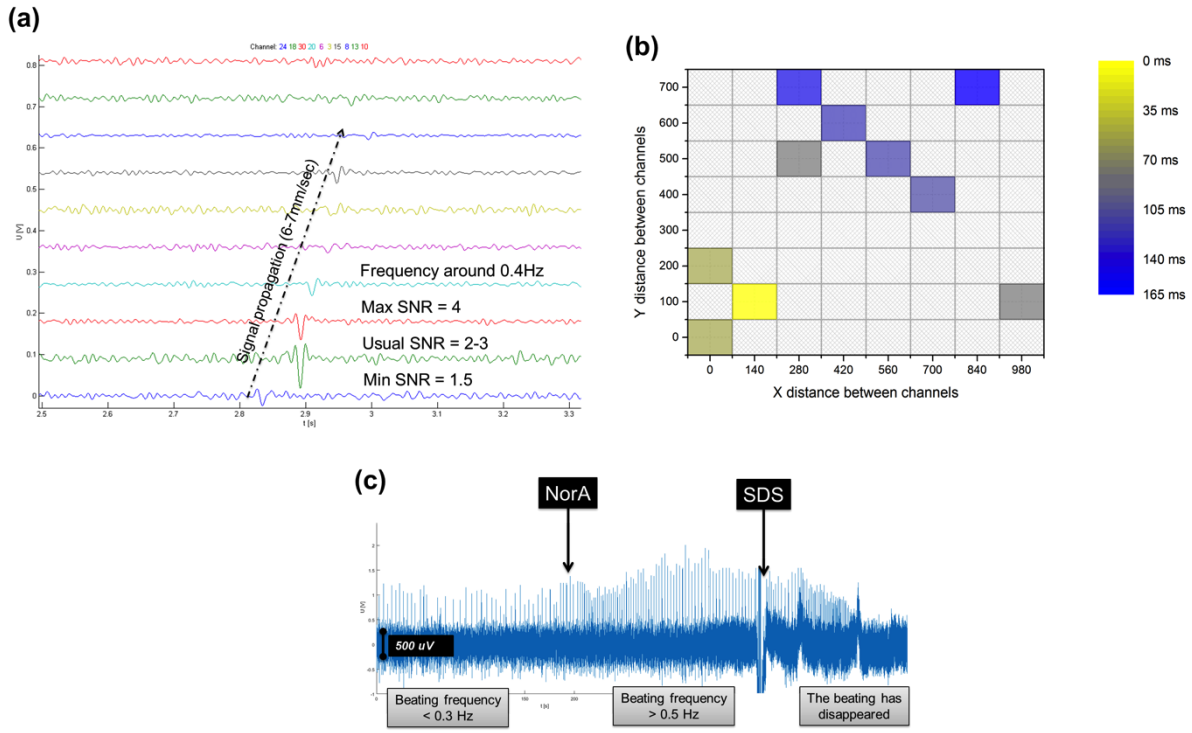

Figure 2 (a) the timetraces of 10 channels with recorded APs; (b) – the heat plot of signal propagation, considering the geometrical locations of the recorded channels; (c) – over 10 minutes long recording with initial APs firing frequency of 0.3Hz, while addition of NorA into the culture medium almost doubles in frequency (>0.5Hz), and SDS slowly "kills" the cells and eventually they stop firing the APs

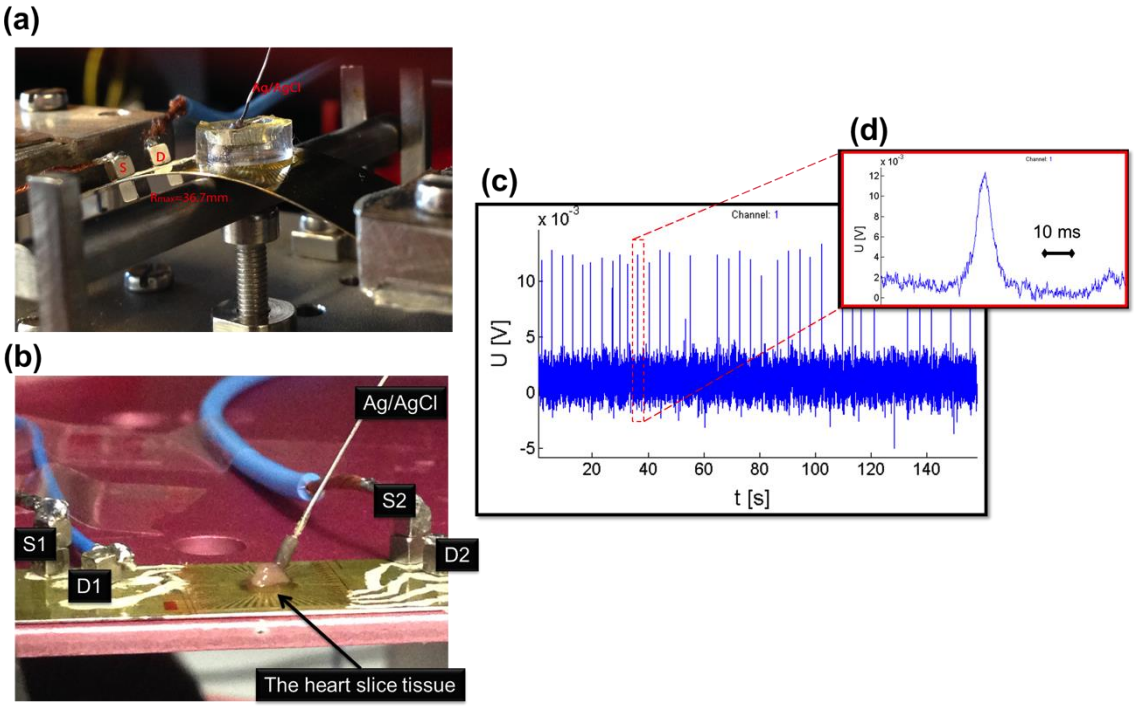

Figure 3 (a) – the flexible and controllably bendable flexible GFETs chip; (b) – the heart slice measurements; (c) – 2.5 minutes long recording of the APs from the heart slice with SNR>5 (unfiltered data); (d) – the close-up of one peak, which is just 10ms wide